REMARKS

This is in response to the Office Action dated March 21, 2006. Claims 1, 10, 16, 17, 20-24, 31, 32, and 45-60 are pending in the above-referenced patent application. Applicants respectfully request further consideration of these claims in view of the following remarks.

Election/Restrictions

The Office action indicates that the new claims 45-60 presented in Amendment A filed November 18, 2005 are directed to an invention that is independent or distinct from the invention originally claimed. The Office action also asserts that Applicants made a constructive election of "the originally presented invention" and that claims 45-60 are withdrawn from consideration as being directed to a non-elected invention. *See* paragraphs 1 and 2 at page 2 of the Office action.

Applicants respectfully traverse the Office's position with regard to the asserted constructive election of invention. Reconsideration thereof is hereby requested for the reasons set forth herein.

Moreover, because the withdrawal of claims 45-60 was improper under 37 C.F.R 1.142(b) and MPEP 821.03, and because the restriction requirement first set forth in the instant Office action is unfair and prejudicial to Applicants, and is improperly applied, Applicants respectfully request that the Office (1) reconsider and make the instant Office action non-final, and (2) reconsider claims 45-60 on the merits in a new supplemental Office action, in view of the remarks herein.

No Constructive Election.

The originally pending claims 1 through 44 included both claims directed to pharmaceutical compositions comprising a core-shell particles (claims 1-36) and to methods of treating an animal subject (claims 37-44). In particular, the originally-filed method claims were directed toward inventions for treating an animal subject to remove potassium ion from the gastrointestinal tract (*See* as-filed claim 43, depending from claim 37), including for renal insufficiency. (*See* as-filed claim 44, depending from claims 43 and 37). In Amendment A, Applicants canceled claims 37-44 in favor of the then-newly added independent method claim 45 and claims 46-60 as depending therefrom.

Therefore, there is no factual basis for the Office's assertion that the prosecution of the claims in Amendment A amounts to a constructive election of the claims drawn to a pharmaceutical composition. The originally filed method claims, although rewritten as new claims in Amendment A, were never

withdrawn by Applicant. As such, the asserted "constructive election" is in error, and the withdrawal of claims 45 through 60 from consideration was improper. *See* 37 C.F.R 1.142(a)

No Previous Restriction and No Previous Express Election

In the previous (and first) Office action dated June 3, 2005, the Office considered all of the pending claims 1 through 44, and did not require restriction between claims 1-36 (pharmaceutical compositions) and claims 37-44 (methods). During an interview with the Examiner on September 15, 2005, the pending claims were discussed.

As such, the instant action is the first restriction requirement being made by the Office. Accordingly, Applicants have not made any previous election of invention.

Restriction After an Office Action on the Merits Is Untimely and Prejudicial to Applicants

Under 37 CFR §1.42(a) and MPEP § 811, a restriction requirement must normally be made before a first action on the merits where the distinctness and independence of the invention is clear.

In the present case, the originally-filed claims were directed to both pharmaceutical compositions and to methods (*See* detailed discussion above). As such, the "different inventions" asserted in the Office action as the basis for restriction were clearly set forth in the claims as filed. Hence, the distinctions relied upon for restriction in the present Office action were already present in the original claims, but yet no restriction was made. Restriction now, after previous Office action on the merits, is untimely.

Moreover, the instant restriction requirement is highly prejudicial to Applicants. Applicants have amended the claims in a good faith effort to advance the prosecution of the case on the merits in response to the previous Office action. As noted above, the amendments to the claims set forth in Amendment A changed the format of the originally-filed claims and, in some cases added or changed requirements, but were otherwise consistent in substance with the original claims. Nonetheless, the previous action did not require restriction. Applicants respectfully submit that such a late-stage restriction requirement is simply unfair, and is highly prejudicial to Applicants. If Applicants are now required to elect between the patentably distinct inventions as set forth in the Office action, (or if the constructive election is not favorably reconsidered by the Office), a divisional case directed to the non-elected claims will lag substantially behind the instant case, and may lose a significant portion of its patent term. The prejudice to Applicants is further heightened in view of the substantial costs involved

in filing, prosecuting and maintaining a second application, particularly in consideration of the relatively small size of Applicants' company, Ilypsa, Inc.

Response to Restriction

In response to the restriction requirement now *first set forth* in this Office action, the Applicants elect, with traverse, independent method claim 45 and dependent claims 46-60 as depending therefrom.

Applicants respectfully traverse the restriction requirement. Under MPEP §803, if the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. In the instant application, although the inventions defined by independent claim 1 (pharmaceutical compositions) and claims depending therefrom are patentably distinct from the inventions defined by independent claim 45 (methods) and claims dependent therefrom, the examination of all of the presently pending claims could be made without serious burden on the Examiner.

Claims 46 through 60 Should Have Been Examined in Any Case.

In any case (*e.g.*, even assuming *arguendo* that the Office's treatment of the instant application with respect to restriction and constructive election was proper), each of claims 46 through 60 should have been examined on the merits. Each of these claims depends from claim 1 (as well as claim 45). The Office action fails to sets forth any basis for not considering the inventions defined by each of these claims as and to the extent depending from claim 1. Accordingly, Applicants request in the alternative that the Office reconsider at least claims 46-60 on the merits in a new supplemental Office action, in view of the remarks herein.

Conclusion.

In conclusion, Applicants respectfully request that the Office (1) reconsider and make the instant Office action non-final, and (2) reconsider claims 45-60 on the merits in a new supplemental Office action, in view of the remarks herein.

Claim Rejections – 35 USC § 112 (Written Description):

The Examiner has rejected claims 1, 10, 16, 17, 20-24, 31, and 32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that "potassium binding polymers are not mentioned in the specification by name or exemplified by the examples." *See* paragraph 3 at pages 2-3 of the Office action.

Applicants respectfully traverse the rejection for the reasons presented below.

Independent claim 1 has been previously amended to require potassium ion as a target solute, to characterize the core component as comprising a potassium-binding cation exchange polymer, to characterize the shell component with as having a higher permeability for potassium ion than for one or more competing cations (*e.g.*, Mg^{++}, Ca^{++}), and to require the core-shell particles to retain bound potassium ion during a period of residence in the gastrointestinal tract of a subject suffering from renal insufficiency or renal failure (*e.g.*, dialysis patients suffering from end stage renal disease). *See* Amendment A filed November 18, 2005.

Generally, the specification describes core-shell compositions that bind target solutes, and describes a preferred embodiment of a target solute as being potassium. See paragraphs [0009] and [0015]. Further potassium binding polymers are clearly and unambiguously described in the specification, include cation exchange polymers having acid functional groups (*e.g.*, carboxylate, phosphonate, sulfate, sulfonate, sulfamate, and combinations thereof). See paragraph [0056].

More particularly, support for the amendments to the claims and for the new claims can be found throughout the as-filed claims, specification and figures, including for example and without limitation: in paragraphs [0008], [0009], [0013] and [0014] (generally); in as-filed claim 43 and in paragraphs [0015] and [0019] (target solute); in paragraph [0018] (competing solute); in paragraphs [0022] and [0056] (core component); in paragraphs [0035] and [0037] through [0041] (shell component); in paragraph [0046] (shell thickness); in paragraphs [0023] through [0034] and [0036] (permeability / permselectivity); in paragraph [0021] (retaining target solute); and in as-filed claims 37, 38, 43 and 44, and in paragraphs [0066] and [0071] (indications).

See also original, as-filed claims of the application directed to pharmaceutical compositions (claims 1-36) and to methods of treatment (claims 37-44), including especially as-filed claim 1 and claims depending therefrom, such as claim 43 (potassium binding, with a mode of action in the gastrointestinal tract), claim 12 (relatively permeability), and claim 44 (renal insufficiency).

Thus, a person of ordinary skill would have readily understood that Applicants were in possession of the invention as defined by the presently pending claims. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claim Rejections – 35 USC § 102:

Tyler et al.

The Examiner has rejected claims 1, 10, 16, 17, 20, 21, 31, and 32 under 35 U.S.C. 102(a, e) as being anticipated by Tyler *et al.* (US 2004/0166156). In the Office action, Tyler *et al.* is said to disclose a core for removing phosphate from the gastrointestinal tract and a coating or shell material with various polymers. The Examiner further asserts that the polymers of Tyler would inherently possess the property of removal of potassium. *See* paragraphs 5 and 6 at pages 3-4 of the Office action.

Applicants respectfully traverse the rejection. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See MPEP § 2131.01. Applicants respectfully assert that the Tyler document does not disclose either expressly or inherently all the requirements of the rejected claims.

In particular, Tyler *et al.* do not disclose a pharmaceutical composition comprising a core-shell particle with a core component comprising a cation exchange resin. Rather, Tyler *et al.* disclose a coated tablet. The coated tablet is disclosed as having a tablet core comprising an aliphatic amine polymer resin, and a water-based coating. *See* paragraph [0007]. The disclosed aliphatic amine polymers are said to be ion exchange resins that are useful to bind phosphate and/or as cholesterol lowering agents (*e.g.*, as a bile acid binder). *See* paragraphs [0002] and [0007] of *Tyler* et al. Hence, Tyler *et al.* disclose only an anion exchange resin as a tablet core.

The Office's reliance on the disclosure in Applicants own specification is misplaced. Although the instant specification discloses amine polymers as core components of core shell particles, the specification is abundantly clear that such embodiments are directed to applications involving anion (*e.g.*, phosphate ion) binding – not to applications involving cation (*e.g.*, potassium ion) binding. A person of ordinary skill in the art would readily understand that Applicants' specification involves different embodiments for different target solutes. *See* for example, paragraph [0015] in which anionic target solutes (including phosphate ions) are delineated separately from cationic target solutes (including potassium ions). In fact, the specification teaches that the core component comprises polymers selected to have functional groups with specific binding properties for a given particular target solute. *See* paragraph [0022] and [0056] of the specification. In this regard, amine functional polymers are disclosed specifically for use as core components of anion binding materials. *See* paragraph [0056]. In

contradistinction, cation exchange polymers disclosed for use as core components include polymers with acid functional groups, such as carboyxylate, among others. *See* paragraph [0056]. As such, the Examiner's rationale in relying on Applicant's own specification for the position that the amine polymers disclosed in Tyler *et al.* are cation exchange resins is without factual basis.

Further, and contrary to the position asserted in the Office action, Tyler *et al.* do not inherently disclose the removal of potassium ion. The Office action asserts that polyallylamine polymers disclosed by Tyler *et al.* would inherently also bind potassium. However, this position is technically inaccurate and legally insufficient. The Office does not set forth any reason why an amine polymer, the amine functional groups of which are provided in an ammonium salt form or which protonoate *in vivo* to an ammonium salt form, would bind potassium. Both ammonium ion and potassium ion are positively charged ions. As such, there is no technical basis to assert an inherent binding. In fact, the electronic properties of such ions would lead to just the opposite – not to any direct association. Since the Office action does not set forth any rationale or extrinsic evidence, it does not set forth a *prima facie* basis establishing the asserted inherency. *See* MPEP §2112. The law is clear that the Examiner must demonstrate that "the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." *See* In re Best, 195 USPQ 430 (CCPA 1977) (emphasis in original); Continental Can Company USA, Inc. v. Monsanto Co., 20 USPQ2d 1746 (Fed. Cir. 1991); *See also* Hansgirg v. Kemmer, 40 USPQ 665, 667 (CCPA 1939) (stating that "(i)nherency may not be established by probabilities or possibilities," but rather, must be based on a "natural result flowing from the operation as taught."). Hence, the asserted inherency basis for the instant rejection is improper.

Additionally, Tyler *et al.* do not disclose core-shell particles that subsist in such core-shell form to retain potassium ion during the period of residence in the gastrointestinal tract. In fact, Tyler *et al.* expressly teach just the opposite. Tyler *et al.* disclose a coated tablet having a tablet core and a water-based coating. *See* paragraph [0007]. The coating is required "for ease of administration to a patient" so that the core polymer does not "swell upon contact with the inside of the mouth." *See* paragraphs [0004] and [0017]. Tyler *et al.* also disclose that the coated tablets should disintegrate to allow for rapid release of the polymer agent from the core. *See* paragraphs [0017] through [0020]; *see also* Example 3 and Figure 1 (disclosing disintegration times). Hence, Tyler *et al.* disclose coated tablets that disintegrate after oral administration to release an active aliphatic amine polymer for binding (with phosphate ions). The binding and retention of a phosphate ion, as disclosed by Tyler *et al.*, involves only a polymer particle; it does not involve a core-shell particle effective as an active pharmaceutical agent to bind

potassium ion and to retain the bound potassium during residence of the core-shell particles in the gastrointestinal tract.

Because Tyler *et al.* do not disclose the claimed inventions, Applicants respectfully request withdrawal of this basis for rejection.

Simon et al.

The Office has also rejected claims 1, 10, 16, 17, 20, 21, 31, and 32 under 35 U.S.C. 102(a, e) as being anticipated by Simon (US 2005/0036983). The Examiner asserts that the particles disclosed in Simon would inherently satisfy the requirements of the claimed invention. *See* paragraphs 7 and 8 at pages 4-5 of the Office action.

Applicants respectfully traverse the rejection for the reasons presented below.

Simon *et al.* disclose an enterically-coated water-absorbing polymer. The enteric coating "protects the polymer from exposure to the stomach", such that "(a)fter passing through the stomach of the host, the coating breaks down wherein the polymer is exposed to the intestinal tract." *See* paragraph [0019]. The enteric coatings "ensure that fluid removal occurs substantially in the intestine rather than the stomach." *See* paragraph [0023].

Simon *et al.* do not anticipate Applicants inventions. In particular, Simon *et al.* do not disclose core-shell particles that subsist in such core-shell form to retain potassium ion during the period of residence in the gastrointestinal tract. Rather, Simon *et al.* disclose a polymer having an enteric coating that breaks down to release the underlying polymer into the intestinal tract. As taught by Simon *et al.*, the released polymer operates as the active pharmaceutical agent; the active agent of Simon *et al.* does not involve a core-shell particle effective as an active pharmaceutical agent to bind potassium ion and to retain the bound potassium during residence of the core-shell particles in the gastrointestinal tract.

Further, the Office's reliance on inherency as to properties of the shell component is misplaced. The Examiner asserts that the there is "no evidence that the polymers recited by Tyler and Simon, and named throughout the specification *would not be capable of* these functional limitations." *See* paragraph 17 at page 7 of the Office Action (emphasis added). However, this is insufficient to establish inherency. The law is abundantly clear that "(i)nherency may not be established by probabilities or possibilities," but rather, must be based on a "natural result flowing from the operation as taught". Hansgirg v. Kemmer, 40 USPQ 665, 667 (CCPA 1939). There is no disclosure or teaching in Simon et al. (or in Tyler *et al.*) from

which a skilled person would necessarily realize, understand or otherwise obtain, as a natural result from such teaching, a shell component comprising a polymer having the property of permeselectivity for potassium ion over a competing ion (*e.g.*, magnesium ion or calcium ion). Accordingly, the Office action does not set forth a *prima facie* basis for inherency. Applicants respectfully request that this basis for rejection be withdrawn.

Claim Rejections – 35 USC § 103:

The Examiner has rejected claims 22-24 under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Tyler et al. (US 2004/0166156), Bandi (US 4,902,501) and Kataoka (US 6,881,484). Applicants respectfully traverse the above rejection.

To establish a prima facie case of obviousness, "the prior art reference (or references when combined) must teach all or suggest all the claim limitations." *See* MPEP 2143. The combination of the Tyler, Bandi, and Kataoka disclosures do not teach all the requirements of the claims defining Applicants' inventions. Claims 22-24 are dependent on independent claims 1 or 45. Claims 1 and 45 each require a pharmaceutical composition comprising a core component, where the core component comprises a cation exchange polymer. As noted above in connection with the anticipation rejection, however, Tyler *et al.* do not expressly or inherently disclose, teach or suggest a cation exchange polymer. Moreover, Tyler *et al.* do not disclose, teach or suggest a disclose core-shell particles that subsist in such core-shell form to retain potassium ion during a period of residence in the gastrointestinal tract. Bandi and Kataoka do not make up for the deficiencies of Tyler *et al.* Accordingly, the Office action does not establish *prima facie* obviousness.

Hence, Applicants respectfully request the withdrawal of this basis for rejection.

Provisional Double Patenting:

The Office action provisionally rejects claims 1, 10, 16, 17 and 20-24 on the ground of nonstatutory obvious-type double patenting over certain claims of co-owned, co-pending US Ser. No. 10/814,749. *See* paragraphs numbered as 2, 3 and 4 [sic: out of sequence due to autoformatting error] at pages 6-7 of the Office action.

Applicants acknowledge the provisional double patenting rejection. Applicants believe that the referenced claims of the instant applications are patentably distinct, in view of specific requirements

recited therein. Nonetheless, Applicants will consider filing a terminal disclaimer to obviate this basis for rejection when the application is otherwise in condition for allowance.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the present application is in form for allowance, and such action is respectfully requested.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 29329-715.202). A duplicate copy of this paper is enclosed.

Respectfully submitted,

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Date: July 21, 2006

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